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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,874	04/19/2005	Ryuji Ueno	Q87423	5640

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EXAMINER	
POLANSKY, GREGG	
ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
05/07/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/531,874	UENO, RYUJI	
	Examiner	Art Unit	
	GREGG POLANSKY	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-13,18,19 and 21-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *25* is/are allowed.

6)☒ Claim(s) *1,3-10,12,13,18,19,21 and 22* is/are rejected.

7)☒ Claim(s) *11,23 and 24* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Applicants' response, filed 4/13/2010, to the Advisory Action mailed 3/18/2010 is acknowledged. Applicants canceled Claim 20, amended Claims 1, 18 and 25, and presented arguments in response to the Advisory Action.

2. Applicants' arguments have been fully considered and are deemed to be persuasive. Rejections and/or objections not reiterated from previous Office actions are hereby withdrawn. Consequently, the finality of the Office action mailed 11/13/2009 is hereby **WITHDRAWN**. The following rejections and objections constitute the complete set presently being applied to the instant application.

3. The election of species requirement of record is hereby WITHDRAWN. Examination has been extended to include the previously non-elected species.

4. Claims 1, 3-13, 18, 19 and 21-25 are pending and presently under consideration.

Claim Objections

5. Claims 11, 23 and 24 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 3, 4, 6, 8, 10 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 recites prostaglandin compounds of formula (I) where "… A is $-CH_3$, or $-CH_2OH$, $-COCH_2OH$, –COOH or **a functional derivative salt, ether, ester or amide thereof** [emphasis added]." See last 2 lines at page 5 of the Claims. The recitation of "a functional derivative salt, ether, ester or amide thereof" lacks clarity. Thus, the metes and bounds of the claim cannot be precisely determined.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3, 4, 6, 8, 10 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter that was not described in the Specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a Written Description rejection.

Claim 18 recites prostaglandin compounds of formula (I) where "… A is $-CH_3$, or $-CH_2OH$, $-COCH_2OH$, –COOH or **a functional derivative salt, ether, ester or amide thereof** [emphasis added]." See last 2 lines at page 5 of the Claims. There is insufficient written basis for "a functional derivative salt, ether, ester or amide thereof" in the Specification.

Regarding the requirement for adequate written description of chemical entities, Applicant's attention is directed to MPEP §2163. In particular, *Regents of the University of California v. Eli Lilly & Co.,* 119 F.3d 1559, 1568 (Fed. Cir. 1997), *cert denied*, 523 U.S. 1089, 118 S. Ct. 1548 (1998), holds that an adequate written description requires a precise definition, such as by structure, formula, chemical name, or physical properties, "not a mere wish or plan for obtaining the claimed chemical invention." *Elli Liily*, 119 F.3d at 1566. The Federal Circuit has adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for Examination of Patent Applications under the 35 U.S.C. 112.1 "Written Description" Requirement ("Guidelines"), 66 Fed. Reg. 1099 (Jan. 5, 2001), which state that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics," including, *inter alia*, "functional characteristics when coupled with a known or disclosed correlation between function and structure…" *Enzo Biochem, Inc. v. Gen-Probe Inc.,* 296 F.3d 316, 1324-25 (Fed. Cir. 2002) (quoting *Guidelines*, 66 Fed. Reg. At 1106 (emphasis added)). Moreover, although *Elli Lilly* and *Enzo* were decided within the factual context of DNA sequences, this does not preclude extending the reasoning of those cases to chemical structures in general. *Univ. of Rochester v. G.D. Searle & Co.*, 249 Supp. 2d 216, 225 (W.D.N.Y. 2003).

Applicant has failed to provide any structural characteristics, chemical formula, name(s) or physical properties of prostaglandin compounds of formula (I) where A is "a functional derivative salt, ether, ester or amide thereof", aside from the broad recitation that such are contemplated for use in the invention. As such, it is not apparent that

Applicant was actually in possession of, and intended to use within the context of the present invention, any specific compounds of formula (I) where A is "a functional derivative salt, ether, ester or amide thereof" at the time the present invention was made. The skilled artisan could not "immediately envisage" the claimed compounds based on the description in the disclosure.

9. Claims 1, 3-10, 12, 13, 18, 19, 21, and 22 are rejected under 35 U.S.C. 112, first paragraph, because the Specification, while being enabling for reducing the weight of obese patients by the administration of prostaglandin E1 (PGE1) compounds as defined by Claims 11 and 23-25, it does not reasonably provide enablement for reducing the weight of obese patients by the administration of multitude of prostaglandin compounds of formula (I) as defined by the rejected claims. The Specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. This is a Scope of Enablement rejection.

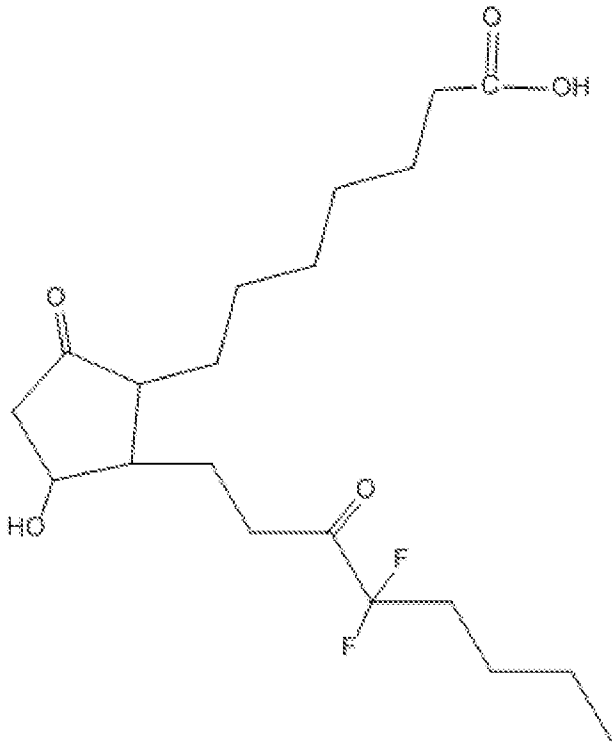
The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on

the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

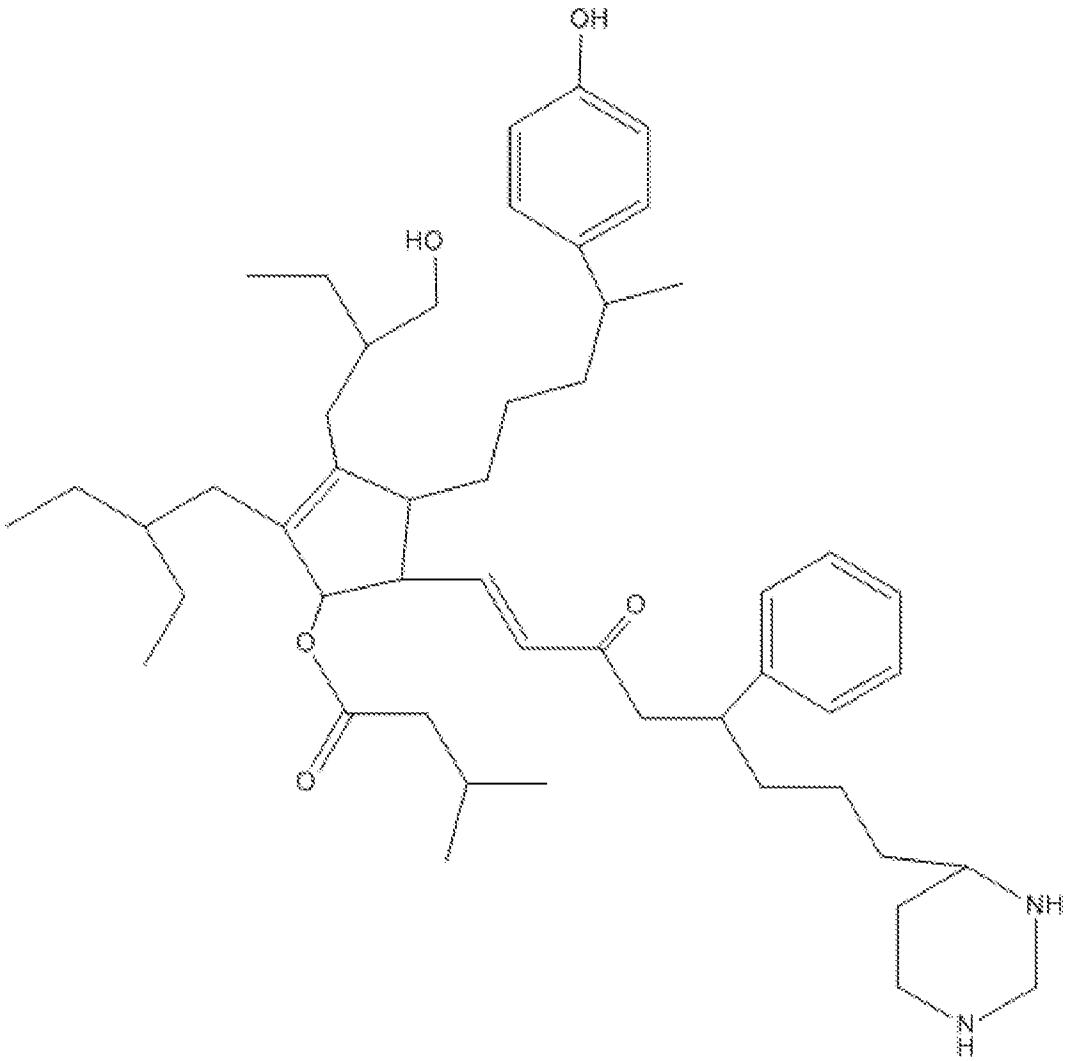
While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

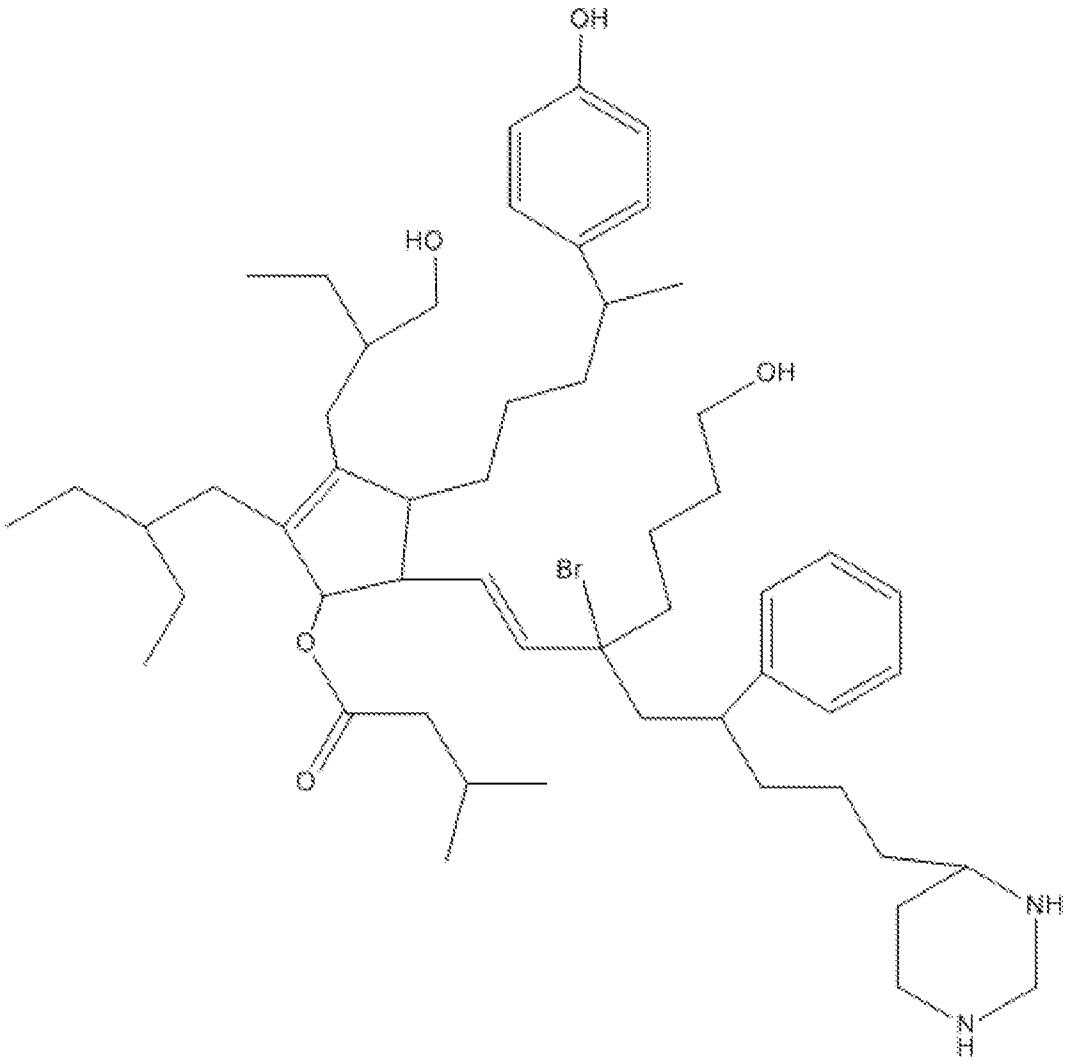
The instant claims are drawn to a method for treating obesity in a subject in need of reduction of body weight, or a method of reducing body weight in a subject in need of treatment for obesity, by administering an effective amount of a prostaglandin compound defined by formula (I) of the claims. The number of compounds defined by formula (I) is very large. The chemical structure of compounds defined by the claims is quite varied. For example, the compound of Claim 25 (13,14-dihydro-15-keto-16,16-difluoro-PGE1), which can be defined by formula (I) of Claim 1, has the following structure ("Structure 1"):


O
C
OH
O
HO
O
F
F

Another compound which can be defined by formula (I) of Claim 1 has the following structure (“Structure 2”):



A compound which can be defined by formula (I) of Claim 18 has the following structure ("Structure 3"):



(3) The state of the prior art:

In arguments presented by Applicants (filed 2/16/2010), Applicants pointed out that the disclosure by Ueno et al. (U.S. Patent No. 5,234,954; previously cited) shows

that administration of the compound 13,14-dihydro-15-keto-16-fluoro-PGE2 to rats does not reduce the body weight of the rats. See columns 17 and 18, including Table 1.

(4) The predictability or unpredictability of the art and (5) the relative skill of those in the art:

The relative skill of those in the art of pharmacology and medicine and the unpredictability of the pharmacological and biological arts are very high. In fact, the courts have made a distinction between mechanical elements, which function the same in different circumstances, yielding predictable results, and chemical and biological compounds, which often react unpredictably under different circumstances. *Nationwide Chem. Corp. v. Wright*, 458 F. supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Aff'd 584 F.2d 714, 200 USPQ 257 (5th Cir. 1978); *In re Fischer*, 427 F.2d 833, 839, 166 USPQ 10, 24(CCPA 1970). Thus, the physiological activity of a chemical or biological compound is considered to be an unpredictable art.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The Specification has provided guidance and a working example for a method of reducing body weight in humans by the oral administration of a single prostaglandin compound, 13,14-dihydro-15-keto-16,16-difluoro-PGE1. This compound differs from the compound of Ueno et al. (i.e., 13,14-dihydro-15-keto-16-fluoro-PGE2; which shows no effect on body weight when administered to rats, *supra*) by the presence

of a second fluorine at position 16, and the substitution of a single bond for a double bond between carbons 5 and 6 (i.e., the compound of Ueno et al. is a PGE2 prostaglandin instead of a PGE1 prostaglandin).

One of skill in the art would not reasonable expect compounds of encompassing the full breadth of the claims, such as, for example, Structure 2 or Structure 3 (*supra*) to have any physiological activity similar to the instantly claimed compound, 13,14-dihydro-15-keto-16,16-difluoro-PGE1 (Structure 1, *supra*); especially when one considers that the comparatively minor change in structures between the instant compound, 13,14-dihydro-15-keto-16,16-difluoro-PGE1, and the compound, 13,14-dihydro-15-keto-16-fluoro-PGE2, disclosed by Ueno et al., results in the loss of weight reduction when administered to subjects.

(8) The quantity of experimentation necessary:

The amount of guidance or direction needed to enable the invention is inversely related to the degree of predictability in the art. *In re Fisher*, 839, 166 USPQ 24. Thus, although a single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements, in cases involving unpredictable factors, such as most chemical reactions and physiological activity, more teaching or guidance is required. *In re Fisher*, 427 F.2d 839, 166 USPQ 24; *Ex Parte Hitzeman*, 9 USPQ 2d 1823. For example, the Federal Circuit determined that, given the unpredictability of the physiological activity of RNA viruses, a specification requires more than a general description and a single embodiment to provide an enabling disclosure for a method of protecting an

organism against RNA viruses. *In re Wright*, 999 F.2d 1562-63, 27 USPQ2d 1575. The Office maintains a very high standard of enablement for claims drawn to methods of prevention. Considering the factors as discussed above, especially the "breadth of the claims", "sufficient working examples", "the level of skill in the art", "the relative skill and the unpredictability in the pharmaceutical art", and the chemical nature of the invention, one of skill in the art would have to undergo an undue amount of experimentation to use the claimed compounds for the claimed methods.

Conclusion

10. Claims 1, 3-10, 12, 13, 18, 19, 21, and 22 are rejected.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GREGG POLANSKY whose telephone number is (571)272-9070. The examiner can normally be reached on Mon-Thur 9:30 A.M. - 7:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gregg Polansky/
Examiner, Art Unit 1614